PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07F 7/08, C08G 18/38 — A1

(11) International Publication Number: **WO 99/03863**

(43) International Publication Date: 28 January 1999 (28.01.99)

(21) International Application Number: PCT/AU98/00546

(22) International Filing Date: 14 July 1998 (14.07.98)

(30) Priority Data:
PO 7878 14 July 1997 (14.07.97) AU

(71) Applicant *(for all designated States except US)*: CARDIAC CRC NOMINEES PTY. LTD. [AU/AU]; Royal North Shore Hospital, Block 4, Level 3, St. Leonards, NSW 2065 (AU).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: GUNATILLAKE, Pathiraja, Arachchillage [AU/AU]; 8 Katoomba Drive, Mulgrave, VIC 3170 (AU). MEIJS, Gordon, Francis [AU/AU]; 3 Henty Street, Murrumbeena, VIC 3163 (AU). ADHIKARI, Raju [NP/AU]; 4/3 Panorama Street, Clayton, VIC 3168 (AU).

(74) Agent: CARTER SMITH & BEADLE; 2 Railway Parade, P.O. Box 557, Camberwell, VIC 3124 (AU).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: SILICON–CONTAINING CHAIN EXTENDERS

$$HO\text{-}R_5\text{-}\underset{\displaystyle R_3}{\overset{\displaystyle R_1}{Si}}\text{-}\left(R_7\text{-}\underset{\displaystyle R_4}{\overset{\displaystyle R_2}{Si}}\right)_n\text{-}R_6\text{-}OH \qquad (I)$$

(57) Abstract

A chain extender including a silicon–containing diol of formula (I) wherein R_1, R_2, R_3, R_4, R_5, and R_6 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical; R_7 is a divalent linking group or an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical; and n is 0 or greater, preferably 2 or less.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

SILICON-CONTAINING CHAIN EXTENDERS

The present invention generally relates to silicon-containing chain extenders and their use in the preparation of polyurethane elastomeric compositions having improved properties. These polyurethane compositions are useful for a variety of applications, in particular the manufacture of medical devices, articles or implants which contact living tissues or bodily fluids.

Polyurethane elastomers are amongst the best performing synthetic polymers in medical implant applications. Their excellent mechanical properties coupled with relatively good biostability make them the choice materials for a number of medical implants including cardiac pacemakers, catheters, implantable prostheses, cardiac assist devices, heart valves and vascular grafts. The excellent mechanical properties of polyurethane elastomers are attributed to their two phase morphology resulting from microphase separation of soft and hard segments. In polyurethanes used for medical implants, the soft segment is typically formed from a polyether macrodiol such as poly(tetramethylene oxide) (PTMO) while the hard segment is derived from a diisocyanate such as 4,4'-methylenediphenyl diisocyanate (MDI) and a diol chain extender such as 1,4-butanediol (BDO).

The diol chain extender which is used to link up diisocyanates is a relatively small difunctional molecule of molecular weight between about 60 and 350. The structure of the chain extender makes a significant contribution to the physical properties of the polyurethane elastomers. The most commonly used diol chain extender is 1,4-butanediol.

Despite the long term use of polyurethane elastomers for applications such as cardiac pacemakers, in some cases the polyurethanes biodegrade causing surface or deep cracking, stiffening, erosion or the deterioration of mechanical

properties such as flexural strength[1]. Elastomers with high flexibility and low Shore A Durometer hardness in particular degrade faster than the harder and more rigid grades. It is generally hypothesized that the degradation is primarily an *in vivo* oxidation process involving the polyether soft segment. The currently used medical polyurethanes are polyether-based and the most vulnerable site for degradation is the methylene group alpha to the ether oxygen[2] of the soft segment. Polyurethanes prepared with a lower amount of polyether component generally exhibit improved degradation resistance. However, such materials typically have high elastic modulus and are difficult to process making them less desirable for many implant applications. Pinchuk has recently reviewed the biostability of polyurethanes[3].

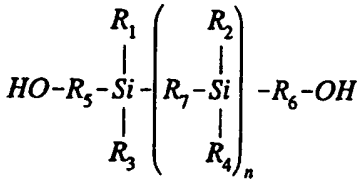
Non-PTMO based polyurethane formulations which show significantly improved *in vivo* degradation resistance as demonstrated by animal implant experiments have also recently been disclosed in the patent literature. These include polyurethane formulations based on polycarbonate macrodiols disclosed in US 5,133,742 (Pinchuk) and US 5,254,662 (Szycher) and polyether macrodiols with fewer ether linkages in US 4,875,308 (Meijs *et al*). The aforementioned patents do not disclose polyurethane formulations which provide materials having flexural modulus, hardness and biostability comparable to those of silicon rubber while retaining high tensile strength, abrasion resistance and tear strength of typical polyurethane elastomers. Although the compositions disclosed in US 5,254,662 provide materials with low elastic modulus and high tensile strength, since those compositions are based on polycarbonate macrodiols and aliphatic diisocyanates, their degradation resistance under *in vivo* conditions is questionable. Hergenrother *et al*[4] have demonstrated by animal implant experiments that aliphatic diisocyanate based polyurethanes degrade more than the aromatic diisocyanate based polyurethanes. There are also no examples provided in US 5,254,662 to demonstrate the biostability of the disclosed low modulus elastomer compositions.

The conventional method of preparing polyurethane elastomers with low hardness and modulus is by formulation changes so as to have a relatively higher percentage of the soft segment component. However, the materials made this way generally have very poor mechanical properties and biostability. For example, it is reported[2,3] that Pellethane 2363-80A (Registered Trade Mark) which has a higher percentage of soft segment than that in the harder grade Pellethane 2363-55D (Registered Trade Mark), is significantly more prone to stress cracking in the biological environment. However, these reports do not disclose methods for formulating polyurethanes with hardness lower than 80 A while retaining good biostability and mechanical properties. Despite the good stability of silicone rubber in biological environments, its use in the medical implant area is limited by poor properties such as low abrasion resistance and low tensile and tear strengths.

Although the aforementioned non-PTMO based polyurethane elastomers address the issue of biostability, they do not provide methods of formulating polyurethanes having properties such as flexibility and biostability comparable to those of silicone rubber. The formulations disclosed in the above patents (except US 5,254,662) typically have hardness in excess of Shore 80 A.

A requirement accordingly exists to develop polyurethanes having properties such as low durometer hardness, low flexural modulus, good processability and high resistance to degradation, without the disadvantages of silicone rubber such as poor tensile strength, abrasion resistance and tear strength. Such polyurethanes should also preferably have a good biostability for applications such as pacemaker leads, vascular grafts, heart valves and the like.

According to one aspect of the present invention there is provided a chain extender including a silicon-containing diol of the formula (I):



(I)

wherein

R_1, R_2, R_3, R_4, R_5, and R_6 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical;

R_7 is a divalent linking group or an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical; and

n is 0 or greater, preferably 2 or less.

The present invention also provides use of the diol of the formula (I) defined above as a chain extender.

The present invention further provides the diol of the formula (I) as defined above when used as a chain extender.

The hydrocarbon radical for substituents R_1, R_2, R_3 and R_4 may include alkyl, alkenyl, alkynyl, aryl or heterocyclyl radicals. It will be appreciated that the equivalent radicals may be used for substituents R_5, R_6 and R_7 except that the reference to alkyl, alkenyl and alkynyl should be to alkylene, alkenylene and alkynylene, respectively. In order to avoid repetition, only detailed definitions of alkyl, alkenyl and alkynyl are provided hereinafter.

The term "alkyl" denotes straight chain, branched or mono- or poly-cyclic alkyl, preferably C_{1-12} alkyl or cycloalkyl. Examples of straight chain and branched alkyl include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, amyl, isoamyl, sec-amyl, 1,2-dimethylpropyl, 1,1-dimethylpropyl,

pentyl, hexyl, 4-methylpentyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, 1,1,2-trimethylpropyl, heptyl, 5-methylhexyl, 1-methylhexyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1,2-dimethylpentyl, 1,3-dimethylpentyl, 1,4-dimethylpentyl, 1,2,3-trimethylbutyl, 1,1,2-trimethylbutyl, 1,1,3-trimethylbutyl, octyl, 6-methylheptyl, 1-methylheptyl, 1,1,3,3-tetramethylbutyl, nonyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-methyloctyl, 1-, 2-, 3-, 4- or 5-ethylheptyl, 1-, 2- or 3-propylhexyl, decyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- and 8-methylnonyl, 1-, 2-, 3-, 4-, 5- or 6-ethyloctyl, 1-, 2-, 3- or 4-propylheptyl, undecyl 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8- or 9-methyldecyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-ethylnonyl, 1-, 2-, 3-, 4- or 5-propyloctyl, 1-, 2- or 3-butylheptyl, 1-pentylhexyl, dodecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-methylundecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- or 8-ethyldecyl, 1-, 2-, 3-, 4-, 5- or 6-propylnonyl, 1-, 2-, 3- or 4-butyloctyl, 1,2-pentylheptyl and the like. Examples of cyclic alkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl and the like.

The term "alkenyl" denotes groups formed from straight chain, branched or mono- or poly-cyclic alkenes including ethylenically mono- or poly-unsaturated alkyl or cycloalkyl groups as defined above, preferably C_{2-12} alkenyl. Examples of alkenyl include vinyl, allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, cyclohexenyl, 1-heptenyl, 3 heptenyl, 1-octenyl, cyclooctenyl, 1-nonenyl, 2-nonenyl, 3-nonenyl, 1-decenyl, 3-decenyl, 1,3-butadienyl, 1,4-pentadienyl, 1,3-cyclopentadienyl, 1,3-hexadienyl, 1,4-hexadienyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl, 1,3,5,7-cycloocta-tetraenyl and the like.

The term "alkynyl" denotes groups formed from straight chain, branched, or mono- or poly-cyclic alkynes. Examples of alkynyl include ethynyl, 1-propynyl, 1- and 2-butynyl, 2-methyl-2-propynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl, 10-undecynyl, 4-ethyl-1-octyn-3-yl, 7-dodecynyl, 9-dodecynyl, 10-dodecynyl, 3-methyl-1-dodecyn-3-yl, 2-tridecynyl, 11-tridecynyl, 3-tetradecynyl, 7-hexadecynyl, 3-octadecynyl and the like.

The term "aryl" denotes single, polynuclear, conjugated and fused residues of aromatic hydrocarbons. Examples of aryl include phenyl, biphenyl, terphenyl, quaterphenyl, phenoxyphenyl, naphthyl, tetrahydronaphthyl, anthracenyl, dihydroanthracenyl, benzanthracenyl, dibenzanthracenyl, phenanthrenyl and the like.

The term "heterocyclyl" denotes mono- or poly-cyclic heterocyclyl groups containing at least one heteroatom selected from nitrogen, sulphur and oxygen. Suitable heterocyclyl groups include N-containing heterocyclic groups, such as, unsaturated 3 to 6 membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl or tetrazolyl; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, such as pyrrolidinyl, imidazolidinyl, piperidino or piperazinyl; unsaturated condensed heterocyclic groups containing 1 to 5 nitrogen atoms, such as, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl or tetrazolopyridazinyl; unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, such as, pyranyl or furyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms, such as, thienyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, oxazolyl, isoazolyl or

oxadiazolyl; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, morpholinyl; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, benzoxazolyl or benzoxadiazolyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as thiazolyl or thiadiazolyl; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as, thiadiazolyl; and unsaturated condensed heterocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as benzothiazolyl or benzothiadiazolyl.

In this specification, "optionally substituted" means that a group may or may not be further substituted with one or more groups selected from oxygen, nitrogen, sulphur, alkyl, alkenyl, alkynyl, aryl, halo, haloalkyl, haloalkenyl, haloalkynyl, haloaryl, hydroxy, alkoxy, alkenyloxy, alkynyloxy, aryloxy, carboxy, benzyloxy, haloalkoxy, haloalkenyloxy, haloalkynyloxy, haloaryloxy, nitro, nitroalkyl, nitroalkenyl, nitroalkynyl, nitroaryl, nitroheterocyclyl, azido, amino, alkylamino, alkenylamino, alkynylamino, arylamino, benzylamino, acyl, alkenylacyl, alkynylacyl, arylacyl, acylamino, acyloxy, aldehydo, alkylsulphonyl, arylsulphonyl, alkylsulphonylamino, arylsulphonylamino, alkylsulphonyloxy, arylsulphonyloxy, heterocyclyl, heterocycloxy, heterocyclylamino, haloheterocyclyl, alkylsulphenyl, arylsulphenyl, carboalkoxy, carboaryloxy, mercapto, alkylthio, arylthio, acylthio and the like.

Suitable divalent linking groups for R_7 include O, S and NR wherein R is hydrogen or an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical.

Preferred silicon-containing diols are 1,3-bis(4-hydroxybutyl)tetramethyl

disiloxane (compound of formula (I) wherein R_1, R_2, R_3 and R_4 are methyl, R_5 and R_6 are butyl and R_7 is O) and 1,4-bis(3-hydroxypropyl)tetramethyl disilylethylene (compound of formula (I) wherein R_1, R_2, R_3 and R_4 are methyl, R_5 and R_6 are propyl and R_7 is ethylene) and 1-4-bis(3-hydroxypropyl)tetramethyl disiloxane.

The silicon-containing diol chain extenders can be conveniently prepared by methods reported in the literature[6]. Some of these compounds such as 1,3-bis(3-hydroxypropyl)tetramethyl disilylethylene (BPTD) and 1,3-bis(4-hydroxybutyl) tetramethyl disiloxane (BHTD) are available commercially. Others can be prepared by using hydrosilylation reaction of the appropriate hydroxy alkene and 1,1,3,3,-tetramethyldisiloxane using a catalyst such as Wilkinson's catalyst.

Some of the diols of formula (I) are novel *per se*. Thus, the present invention also provides a silicon-containing diol of the formula (I) defined above wherein R_7 is ethylene.

In a preferred embodiment, the diol of the formula (I) defined above is combined with a chain extender known in the art of polyurethane manufacture.

According to another aspect of the present invention provides a chain extender composition including a silicone-containing diol of the formula (I) defined above and a chain extender known in the art of polyurethane manufacture.

The present invention also provides use of the composition defined above as a chain extender.

The present invention further provides the composition defined above when used as a chain extender.

The chain extender known in the art of polyurethane manufacture is preferably selected from 1,4-butanediol, 1,6-hexanediol, 1,8-octanediol, 1,9-nonanediol, 1,10-decanediol, 1,12-dodecanediol, 1,4-cyclohexanedimethanol, p-xylene glycol and 1,4-bis(2-hydroxyethoxy) benzene. 1,4 butanediol is particularly preferred.

The silicon chain extender and the known chain extender can be used in a range of molar proportions with decreasing tensile properties as the molar percentage of the silicon chain extender increases in the mixture. A preferred molar percentage of silicon chain extender is about 1 to about 50%, more preferably about 40%.

Although the preferred chain extender composition contains one known chain extender and one silicon-containing diol, it will be understood that mixtures containing more than one known chain extender and diol may be used in the chain extender composition.

The chain extender and chain extender composition of the present invention are particularly useful in preparing polyurethane elastomeric compositions.

According to a still further aspect of the present invention there is provided a polyurethane elastomeric composition which includes a chain extender or chain extender composition defined above.

The polyurethane elastomeric compositions of the present invention may be prepared by any suitable known technique. A preferred method involves mixing the chain extender or chain extender composition with a soft segment

macrodiol and then reacting this mixture with a diisocyanate. The initial ingredients are preferably mixed at a temperature in the range of about 45 to about 100°C, more preferably about 60 to about 80°C. If desired, a catalyst such as dibutyl tin dilaurate at a level of about 0.001 to about 0.5 wt % based on the total ingredients may be added to the initial mixture. The mixing may occur in conventional apparatus or within the confines of a reactive extruder or continuous reactive injection molding machine.

Alternatively, the polyurethanes may be prepared by the prepolymer method which involves reacting a diisocyanate with the soft segment macrodiol to form a prepolymer having terminal reactive diisocyanate groups. The prepolymer is then reacted with the chain extender or chain extender composition.

Thus, the polyurethane elastomeric composition of the present invention may be further defined as comprising a reaction product of:

(i) a soft segment macrodiol;

(ii) a diisocyanate; and

(iii) the chain extender or chain extender composition defined above.

The soft segment macrodiol may be of any suitable type known in the art of polyurethane manufacture. Examples include polyethers, polyesters, polysiloxanes, polycarbonates or mixtures thereof. Preferably, the soft segment is derived from a polysiloxane macrodiol and a polyether macrodiol.

A suitable polysiloxane is polydimethyl siloxane (PDMS). The polysiloxane macrodiols may be obtained as commercially available products such as X-22-160AS from Shin Etsu or prepared according to known procedures[7]. The preferred molecular weight range of the polysiloxane macrodiol is about 200

to about 5000, more preferably about 300 to about 1200.

Suitable polyether macrodiols include those represented by the formula (II)

$$HO\text{-}\left[(CH_2)_m\text{-}O\right]_n\text{-}H$$

(II)

wherein

m is an integer of 5 or more, preferably 5 to 18; and

n is an integer of 2 to 50.

Although conventional polyether macrodiols such as PTMO can be used, the more preferred macrodiols and their preparation are described in Gunatillake *et al*[8] and US 5403912. Polyethers such as PHMO described in these references are more hydrophobic than PTMO and are more compatible with polysiloxane macrodiols. The preferred molecular weight range of the polyether macrodiol is about 200 to about 5000, more preferably about 200 to about 1200.

Preferably, the diisocyanate is selected from 4,4'-methylenediphenyl diisocyanate (MDI), methylene bis (cyclohexyl) diisocyanate (H12MDI), p-phenylene diisocyanate (p-PDI), trans-cyclohexane-1, 4-diisocyanate (CHDI) or a mixture of the cis and trans isomers, 1,6-hexamethylene diisocyanate (DICH), 2,4-toluene diisocyanate (2,4-TDI) or its isomers or mixtures thereof, p-tetramethylxylene diisocyanate (p-TMXDI) and m-tetramethylxylene diisocyanate (m-TMXDI). MDI is particularly preferred.

A particularly preferred polyurethane elastomeric composition of the present invention comprises a reaction product of:

(i) macrodiols including:

(a) polysiloxane macrodiol; and

(b) polyether macrodiol;

(ii) MDI; and

(iii) chain extender composition including 1,4-butanediol and a silicon chain extender selected from 1,3-bis(4-hydroxybutyl)tetramethyl disiloxane and 1,4-bis(3-hydroxypropyl)tetramethyl disilylethylene and 1-4-bis(3-hydroxypropyl)tetramethyl disiloxane..

Preferably, the silicon chain extender is present in an amount of about 40 mol % of the chain extender composition.

The methods described above do not cause premature phase separation and yield polymers that are compositionally homogeneous and transparent having high molecular weights. These methods also have the advantage of not requiring the use of any solvent to ensure that the soft and hard segments are compatible during synthesis.

The polyurethane may be processed by conventional methods such as extrusion, injection and compression moulding without the need of added processing waxes. If desired, however, conventional polyurethane processing additives such as catalysts, antioxidants, stablisers; lubricants, dyes, pigments, inorganic and/or organic fillers and reinforcing materials can be incorporated into the polyurethane during preparation. Such additives are preferably added to the soft segment macrodiol.

The soft segment macrodiol, diisocyanate and the chain extender or chain extender composition may be present in certain preferred proportions. The preferred level of hard segment (i.e. diisocyanate and chain extender) in the composition is about 40 to about 60 wt%. The weight ratio of polysiloxane to polyether in the preferred soft segment may be in the range of from 1:99

to 99:1. A particularly preferred ratio of polysiloxane to polyether which provides increased degradation resistance, stability and clarity is 80:20.

The polyurethane elastomeric composition of the present invention is particularly useful in preparing materials having good mechanical properties, in particular biomaterials.

According to another aspect of the present invention there is provided a material having improved mechanical properties, clarity, processability and/or degradation resistance comprising a polyurethane elastomeric composition which includes a chain extender or chain extender composition defined above.

The present invention also provides use of the polyurethane elastomeric composition defined above as a material having improved mechanical properties, clarity, processability and/or degradation resistance.

The present invention further provides the polyurethane elastomeric composition defined above when used as a material having improved mechanical properties, clarity, processability and/or degradation resistance.

The mechanical properties which are improved include tensile strength, tear strength, abrasion resistance, Durometer hardness, flexural modulus and related measures of flexibility or elasticity.

The improved resistance to degradation includes resistance to free radical, oxidative, enzymatic and/or hydrolytic processes and to degradation when implanted as a biomaterial.

The improved processability includes ease of processing by casting such as

solvent casting and by thermal means such as extrusion and injection molding, for example, low tackiness after extrusion and relative freedom from gels.

There is also provided a degradation resistant material which comprises the polyurethane elastomeric composition defined above.

The polyurethane elastomeric composition of the present invention shows good elastomeric properties. It should also have a good compatibility and stability in biological environments, particularly when implanted *in vivo* for extended periods of time.

According to another aspect of the present invention there is provided an *in vivo* degradation resistant material which comprises the polyurethane elastomeric composition defined above.

The polyurethane elastomeric composition may also be used as a biomaterial. The term "biomaterial" is used herein in its broadest sense and refers to a material which is used in situations where it comes into contact with the cells and/or bodily fluids of living animals or humans.

The polyurethane elastomeric composition is therefore useful in manufacturing medical devices, articles or implants.

Thus, the present invention still further provides medical devices, articles or implants which are composed wholly or partly of the polyurethane elastomeric composition defined above.

The medical devices, articles or implants may include cardiac pacemakers, defibrillators and other electromedical devices, catheters, cannulas,

implantable prostheses, cardiac assist devices, heart valves, vascular grafts, extra-corporeal devices, artificial organs, pacemaker leads, defibrillator leads, blood pumps, balloon pumps, A-V shunts, biosensors, membranes for cell encapsulation, drug delivery devices, wound dressings, artificial joints, orthopaedic implants and soft tissue replacements.

It will be appreciated that polyurethane elastomeric compositions having properties optimised for use in the construction of various medical devices, articles or implants will also have other non-medical applications. Such applications may include their use in the manufacture of artificial leather, shoe soles; cable sheathing; varnishes and coatings; structural components for pumps, vehicles, etc; mining ore screens and conveyor belts; laminating compounds, for example in glazing; textiles; separation membranes; sealants or as components of adhesives.

Thus, the present invention extends to the use of the polyurethane elastomeric composition defined above in the manufacture of devices or articles.

The present invention also provides devices or articles which are composed wholly or partly of the polyurethane elastomeric composition defined above.

The invention will now be described with reference to the following examples. These examples are not to be construed as limiting the invention in any way.

In the examples, reference will be made to the accompanying drawings in which:

Figures 1a and 1b are two photomicrographs of a polyurethane composition

in Example 1 explanted after three months; and

Figures 2a and 2b are two micrographs of a commercial Pellethane 2363-55D explanted after three months.

Example 1

A polyurethane composition based on a mixture of PDMS/PHMO, a mixture of BDO and BHTD, and MDI was prepared by a one-step bulk polymerisation procedure.

α,ω-bis (6-hydroxyethoxypropyl)polydimethylsiloxane (Shin Etsu product x-22-160AS, MW 940.27) (PDMS) containing 0.1 wt% of tris(nonyltriphenyl)phosphine (TNPP) was dried at 105°C for 15 h under vacuum (0.1 torr). Poly(hexamethylene oxide) (PHMO), prepared according to a method described by Gunatillake *et al*[8] and US 5403912, was dried at 130°C with 0.1 wt% TNPP (based on PHMO weight) under vacuum (0.1 torr) for 4 h. The molecular weight of the PHMO was 851.54. BHTD was degassed under vacuum (0.1 torr) at ambient temperature immediately before use to remove the cyclic impurities.

A mixture of dried PDMS (260.0 g), PHMO (65.00 g), 1,4-butanediol (16.14 g), dibutyl tin dilaurate catalyst (0.054 g), Irgawax (0.81 g) and Irganox 1010 (0.54 g) was placed into a 1L flask and degassed at 80°C for 2 h under vacuum (0.2 torr). Separately degassed BHTD (33.256 g) was added to the flask containing the macrodiol mixture. This mixture (370.00 g) was weighed into a 1L polypropylene beaker and allowed to cool to 70°C under nitrogen. Molten MDI (164.67 g) at 60°C was weighed in a fume hood into 250 ml polypropylene beaker. The MDI was then quickly added with rapid stirring using a stainless steel spatula. The mixture, which was initially cloudy, turned clear with mixing after about 10 sec. The viscous mixture

was rapidly poured onto a teflon coated metal tray and cured in an oven under nitrogen at 100°C. Heating was discontinued after 4 h and the sheet of polyurethane was allowed to cool to ambient temperature over a period of about 15 h.

A sample of the polymer after drying for 15 h at 45°C under vacuum (0.1 torr) was compression moulded at 180°C to a 1mm thick flat sheet for tensile testing. Dumbbells punched from the sheet were tensile tested using an Instron Model 4032 Universal Testing Machine.

The degradation resistance of the polyurethane composition described in example 1 was examined by a three month ovine implant experiment.

Polyurethane in example 1, Pellethane 2363-80A (Registered Trade Mark) and 2363-55D were compression moulded into sheets of 0.5 mm thickness. Specimens shaped as dumbbells were cut from the sheets and stretched over poly(methyl methacrylate) holders. This caused the central section to be strained to 250% of its original length. A polypropylene suture was firmly tied around the centre of each specimen. This caused a localised increase in stress in the specimen. The specimens attached to their holders were sterilised with ethylene oxide and implanted into the subcutaneous adipose tissue in the dorsal thoraco-lumbar region of adult crossbred wether sheep. This test method provides a means of assessing the resistance to biodegradation by environmental stress cracking.

After a period of three months the polyurethanes were retrieved. Attached tissue was carefully dissected away and the specimens were washed by soaking in 0.1M sodium hydroxide for 2 days at ambient temperature followed by rinsing in deionised water. The specimens were then dried in air and examined by scanning electron microscopy (SEM) for signs of pitting

or cracking. The polyurethane sample showed no sign of stress cracking and while Pellethane 80A showed severe degradation. Since Pellethane 80A showed severe degradation visible to the naked eye, those samples were not examined by SEM. Representative scanning photomicrographs of the new polyurethane composition and Pellethane 55D are shown in Figures 1 and 2, respectively.

The mechanical properties of the material prepared in example 1 were examined and the results are shown in Table 1 with those of Pellethane 2363-80A (Registered Trade Mark) for comparison.

Table 1

Property	Polyurethane -example 1	Prior art soft Polyurethane (Pellethane - 2363A 8OA)+
Shore Hardness	70A	82A
Ultimate Tensile (MPa)	28	33.7
Elongation at break	420	430
Young's Modulus (MPa)	9.6	13
Tear Strength ($N.mm^{-1}$)	51	72
Flexural Modulus (MPa)	14	26

+ Results from testing of a commercial sample of Pellethane 2363-80A

The thermal processability of the polyurethane elastomer prepared according to the procedure in example 1 was evaluated by extrusion into a thin film (0.5 mm) using a single screw Brabender extruder. The polyurethane was dried at 45°C under vacuum (0.1 torr) for 48 h prior to the extrusion. The material extruded easily into a clear and transparent film with no imperfections and the post extrusion tackiness was minimal with easy handling.

Example 2

A polyurethane composition based on a mixture of PDMS/PHMO, a mixture of BDO and BHTD, and MDI was prepared by a two-step bulk polymerisation procedure without the use of the catalyst or other conventional additives used in example 1. The composition was based on an isocyanate index ([NCO/[OH]) of 1.03 and a hard segment weight percentage of 40.

PDMS (Shin Etsu product X-22-160AS, MW 937.83) was dried at 105°C for 15h under vacuum (0.1 torr). PHMO (MW 696.06) was dried at 130°C under vacuum (0.1 torr) for 4 h prior to polymerisation.

Molten MDI (195.0 g) was weighed into a 2 L three necked round bottom flask fitted with an additional funnel, nitrogen inlet and a mechanical stirrer. The dried polyol mixture (240.0 g PDMS and 60.0 g PHMO) was weighed into the additional funnel and then added to MDI in the flask over a period of 30 min with stirring. During this time the reaction temperature was maintained at 70°C. The reaction was continued for further 2 h at 80°C with stirring to form the prepolymer. The prepolymer (537.1 g) was then weighed into a 2 L polypropylene beaker and thoroughly mixed with the chain extenders BDO (16.82 g) for 2 min. The polymer was poured into a teflon coated pan and cured at 100°C for 4 h in an oven under nitrogen.

The cured polyurethane after drying at 45°C under vacuum (0.1 torr) was compression moulded at 180°C into 2 mm thick flat sheets for testing tensile properties and flexural modulus, and 2 mm thick, 10.5 cm diameter discs for abrasion resistance. Tensile properties and flexural strength were tested on an Instron Model 4032 Universal Testing Machine while the abrasion resistance was tested on a Taber Model 503 Abraser using Calibrade H-22 abrading wheels and 1000 g wheel loading. The tensile test specimens were 10 cm long dumbbells with a 6 mm wide narrow section. The test results are summarised in Table 2 along with corresponding properties for a commercial sample of silicon rubber. Some properties of high tear strength silicon rubber as reported in the literature[5] are shown in Table 3 for comparison.

The clarity of the polyurethane composition in example 2 and commercial silicone rubber was measured on a Gardner Hazemeter Model UX10, using 2

mm thick films.

Table 2

Property	Polyurethane of example 2	Silicon Rubber†
Durometer Hardness (Shore A)	70	65
Tensile Strength (MPa)	20	9.0
Elongation at Break (%)	890	410
Young's Modulus (MPa)	4.4	5.0
Tear Strength (n/mm)	57	45
Flexural Modulus (MPa)	14	17
Abrasion (depth (mm)/3000 revolutions)	0.06	0.09

† Results from testing of a commercial sample of Silicon Rubber

Table 3

Property	Silicon Rubber		
	1	2	3
Durometer Hardness (Shore A)	50	50	50
Tensile Strength (MPa)	6.90	10.34	9.66
Tear Strength (N/mm) (ASTM D624-54, Disc B)	17.50	33.25	35.00
Abrasion (Rev/0.254 cm) (ASTM D1630 61)	155	300	1600

Table 4

Sample	Hazemeter Reading (% absorption)
Polyurethane of Example 2	7
Commercial silicon rubber	65
Clear glass (microscope slide)	1.5
Parafilm	50

The results in Tables 2, 3 and 4 clearly demonstrate that the composition of the present invention are superior to silicon rubber with respect to tensile strength, tear strength and abrasion resistance as well as film clarity.

Example 3

1,4-bis(3-hydroxypropyl)-1,1,4,4-tetramethyl disilylethylene (HTDE) was prepared by a hydrosilylation procedure.

1,1,4,4,-Tetramethyldisilylethylene (50.0 g) and tris(triphenylphosphine) rhodium chloride (Wilkinson's catalyst, 0.005 g) were placed in a 500 ml round bottom flask fitted with a nitrogen inlet, addition funnel, a drying tube and a condenser. The flask was placed in an oil bath at 40°C and allylalcohol (80.00 g) was added to the reaction mixture over a period of 30 min. After the addition was completed, the oil bath temperature was raised to 80°C and continued reaction for 2 h. A sample of the reaction was analysed by IR spectroscopy. The absence of an Si-H band at 2160 cm^{-1} was taken as the completion of the reaction. The product mixture was dissolved in CH_2Cl_2 and treated with charcoal to remove the catalyst. The product was purified by vacuum distillation and the fraction distilled at 135-137°C/0.1 torr was used for the preparation of polyurethane.

PDMS and PHMO were purified according to the procedures described in Example 1. PDMS (28.00 g), PHMO (7.00 g), BDO (2.433 g), HTDE (2.363 g) and dibutyl tin dilauarate (0.006 g) were weighed into a 100 ml poly(propylene) beaker and degassed at 80°C for 2 h under vacuum (2 torr). Molten MDI (18.57 g) was quickly added to the contents in the beaker and stirred rapidly. The polymer was cured in the beaker at 100°C for 4 h in an oven under nitrogen.

A sample of the polymer after drying for 15 h at 45°C under vacuum (0.1 torr) was compression moulded at 180°C to a 1 mm thick flat sheet for tensile testing. Dumbbells punched from the sheet were tensile tested on an Instron Model 4032 Universal Testing Machine: fail stress 17 MPa, fail strain 460%, Young's modulus 17.6 MPa, Shore hardness 79A and tear strength 51 N/mm.

Example 4

1,3-bis(5-hydroxypentyl)-1,1,3,3-tetramethyldisiloxane (BHPD) and 1,3-bis(6-hydroxyhexyl)-1,1,3,3-tetramethyldisiloxane (BHHD) were prepared using procedures similar to that described in example 3.

Two polyurethanes were prepared using a one step procedure similar to that described in example 1. The polyurethane based on BHPD was prepared from PDMS (20.0 g), PHMO (5.0 g), MDI (12.72 g), BDO (1.209 g), BHPD (2.742 g) and catalyst dibutyl tin dilaurate (0.004 g). Likewise, a polyurethane based on BHHD was prepared from PDMS (20.0 g), PHMO (5.0 g), MDI (12.57 g), BDO (1.178 g), BHHD (2.914 g) and dibutyl tin dilaurate (0.004 g).

Samples of the two polymers after drying for 15 h at 45°C under vacuum

(0.1 torr) were compression moulded at 180°C to a 1 mm thick flat sheet for testing tensile properties. Dumbbells punched from the sheets were tested on an Instron Model 4032 Universal Testing Machine. The polyurethane based on BHPD showed fail stress 19.5 MPa, fail strain 300%, stress at 100% elongation 7.2 MPa, Shore Hardness 67A and Young's modulus 11.2 MPa. Similarly, the polyurethane based on BHHD showed fail stress 22.2 MPa, fail strain 290%, Shore Hardness 60A and Young's modulus 12.7 MPa.

Example 5

PDMS and PHMO were purified according to the procedures described in Example 1. PDMS (5.00 g), PHMO (20.0 g), BDO (2.04 g), BHTD (4.203 g) and dibutyl tin dilaurate (0.005 g) were weighed into a 100 ml poly(propylene) beaker and degassed at 80°C for 2 h under vacuum (2 torr). Hydrogenated MDI (Aldrich, 18.76 g) was quickly added to the contents in the beaker and stirred rapidly. The polymer was cured in the beaker at 100°C for 4 h in an oven under nitrogen.

The polymer after curing was colourless and transparent. A 1 mm thick sheet of the polymer was prepared by compression moulding at 180°C. Dumbbells punched from the sheet were tested for tensile properties on an Instron Model 4032 Universal Testing Machine: fail stress 18 MPa, fail strain 410%, stress at 100% elongation 2.3 MPa, Young's modulus 10 MPa and Shore hardness 60A.

Example 6

This example illustrates the synthesis of a polyurethane composition using a PDMS macrodiol with a molecular weight of 1913.3 according to a two-step polymerisation procedure.

MDI (23.85g) was weighed into a 250mL three necked round bottom flask fitted with a dry nitrogen inlet, a mechanical stirrer and an addition funnel. The reaction flask was placed in an oil bath at 70°C and the polyol mixture (40.00g, PDMS molecular weight 1913.3 and 10.00g PHMO, molecular weight 700.16) was slowly added to MDI from the addition funnel over a period of 15 min. After completion of the addition, the oil bath temperature was raised to 80°C and reacted for 2 hours with stirring under a slow flow of nitrogen to complete the reaction. The prepolymer was then dissolved in anhydrous N,N-dimethyformamide (DMF) (440mL) to make a 15% solution. The chain extender mixture, 1,4-butanediol (3.099g) and 1,3bis(4-hydroxybutyl)tetramethyl disiloxane (6.387g), was added to the prepolymer solution and reacted at 90°C for 4h with stirring.

A 0.5mm thick film was cast from the DMF solution of the polymer onto a Petrie dish and dried at 45°C in an over for 48h to remove the solvent. The cast film was clear and transparent. Test specimens were punched from the film for testing tensile properties and tear strength.

The polyurethane exhibited 22 MPa fail stress, 440% fail strain, 15 MPa Young's modulus, and 7 MPa stress at 100% elongation. The tear strength of the polyurethane was 60 N/mm.

References

1. M. Szycher, *J. Biomat. Appl.*, Vol 3, pp 297-402, (1988).
2. M. Szycher and W.A. McArthur, Surface Fissuring of Polyurethanes Following *In Vivo* Exposure, In A.C. Fraker and C.D. Griffin, Eds. *Corrosion and Degradation of Implant Materials*, Philadelphia, PA, ASTM STP 859, pp 308-321, (1985).
3. L. Pinchuk, *J. Biomater. Sci. Edn*, Vol 3 (3), pp 225-267, (1994).
4. R.W. Hergenrother and S.L. Cooper, *Mat. Res. Soc. Symp. Proc.*, Vol

252, pp 257-263, (1992).

5. K.E. Polmanteer, Advances in Silicon Rubber Technology in *Handbook of Elastomers*, A.K. Bhowmick and H.L. Stephens, Eds Marcel Dekker, Inc., pp 551-615, (1988).

6. F. Braun, L. Willner, M. Hess and R. Kosfeld, *J.Organomet. Chem.*, Vol 332, pp 63-68, (1987).

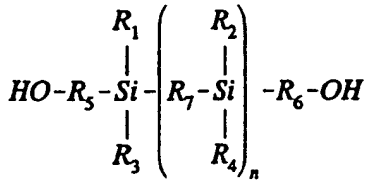
7. I. Yilgor, J.S. Riffle, W.P. Steckle, Jr., A.K. Banthia and J.E. McGrath, *Polym. Mater. Sci & Eng.*, Vol 50, pp 518-522, (1984).

8. P.A. Gunatillake, G.F. Meijs, R.C. Chatelier, D.M. McIntosh and E. Rizzardo, *Polym. Int.*, Vol 27, pp 275-283, (1992).

It will be appreciated that further modifications and alterations may be made to the embodiment described above without departing from the scope or spirit of the present invention.

CLAIMS:

1. A chain extender including a silicon-containing diol of the formula (I):



(I)

wherein

R_1, R_2, R_3, R_4, R_5, and R_6 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical;

R_7 is a divalent linking group or an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical; and

n is 0 or greater, preferably 2 or less.

2. A chain extender as claimed in claim 1 wherein R_1, R_2, R_3 and R_4 are the same or different and are selected from alkyl, alkenyl, alkynyl, aryl or heterocycle radicals.

3. A chain extender as claimed in claim 2 wherein said alkyl radicals include straight chain, branched or mono- or poly- cyclic alkyl radicals.

4. A chain extender as claimed in claim 3 wherein said alkyl radicals are selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, amyl, isoamyl, sec-amyl, 1,2-dimethylpropyl, 1,1-dimethylpropyl, pentyl, hexyl, 4-methylpentyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, 1,1,2-trimethylpropyl, heptyl, 5-methylhexyl, 1-methylhexyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1,2-dimethylpentyl, 1,3-dimethylpentyl, 1,4-dimethylpentyl,

1,2,3-trimethylbutyl, 1,1,2-trimethylbutyl, 1,1,3-trimethylbutyl, octyl, 6-methylheptyl, 1-methylheptyl, 1,1,3,3-tetramethylbutyl, nonyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-methyloctyl, 1-, 2-, 3-, 4- or 5-ethylheptyl, 1-, 2- or 3-propylhexyl, decyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- and 8-methylnonyl, 1-, 2-, 3-, 4-, 5- or 6-ethyloctyl, 1-, 2-, 3- or 4-propylheptyl, undecyl 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8- or 9-methyldecyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-ethylnonyl, 1-, 2-, 3-, 4- or 5-propyloctyl, 1-, 2- or 3-butylheptyl, 1-pentylhexyl, dodecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- or 10-methylundecyl, 1-, 2-, 3-, 4-, 5-, 6-, 7- or 8-ethyldecyl, 1-, 2-, 3-, 4-, 5- or 6-propylnonyl, 1-, 2-, 3- or 4-butyloctyl, 1,2-pentylheptyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl and cyclodecyl.

5. A chain extender as claimed in any one of claims 2 to 4 wherein said alkenyl radicals include groups formed from straight chain, branched or mono- or poly-cyclic alkenes.

6. A chain extender as claimed in claim 5 wherein said alkenyl radicals include vinyl, allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, cyclohexenyl, 1-heptenyl, 3 heptenyl, 1-octenyl, cyclooctenyl, 1-nonenyl, 2-nonenyl, 3-nonenyl, 1-decenyl, 3-decenyl, 1,3-butadienyl, 1,4-pentadienyl, 1,3-cyclopentadienyl, 1,3-hexadienyl, 1,4-hexadienyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl and 1,3,5,7-cycloocta-tetraenyl.

7. A chain extender as claimed in any one of claims 2 to 6 wherein said alkynyl radicals include groups formed from straight chain, branched or mono- or poly-cyclic alkenes.

8. A chain extender as claimed in claim 7 wherein said alkynyl radicals

include ethynyl, 1-propynyl, 1- and 2-butynyl, 2-methyl-2-propynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl, 10-undecynyl, 4-ethyl-1-octyn-3-yl, 7-dodecynyl, 9-dodecynyl, 10-dodecynyl, 3-methyl-1-dodecyn-3-yl, 2-tridecynyl, 11-tridecynyl, 3-tetradecynyl, 7-hexadecynyl and 3-octadecynyl.

9. A chain extender as claimed in any one of claims 2 to 8 wherein said aryl radicals include single, polynuclear, conjugated and fused residues of aromatic hydrocarbons.

10. A chain extender as claimed in claim 9 wherein said aryl radicals include phenyl, biphenyl, terphenyl, quaterphenyl, phenoxyphenyl, naphthyl, tetrahydronaphthyl, anthracenyl, dihydroanthracenyl, benzanthracenyl, dibenzanthracenyl and phenanthrenyl.

11. A chain extender as claimed in any one of claims 2 to 10 wherein said heterocycle radicals include mono- or poly-cyclic heterocycle groups containing at least one heteroatom selected from nitrogen, sulphur and oxygen.

12. A chain extender as claimed in claim 11 wherein said heterocycle radicals include N-containing heterocyclic groups, such as, unsaturated 3 to 6 membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl or tetrazolyl; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, such as pyrrolidinyl, imidazolidinyl, piperidino or piperazinyl; unsaturated condensed heterocyclic groups containing 1 to 5 nitrogen atoms, such as, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl or tetrazolopyridazinyl; unsaturated 3 to 6-membered

heteromonocyclic group containing an oxygen atom, such as, pyranyl or furyl; unsaturated 3 to 6-membered hetermonocyclic group containing 1 to 2 sulphur atoms, such as, thienyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, oxazolyl, isoazolyl or oxadiazolyl; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, morpholinyl; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, benzoxazolyl or benzoxadiazolyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as thiazolyl or thiadiazolyl; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as, thiadiazolyl; and unsaturated condensed heterocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as benzothiazolyl or benzothiadiazolyl.

13. A chain extender as claimed in any one of claims 1 to 12 wherein R_5, R_6 and R_7 are the same or different and are selected from alkylene, alkenylene, alkynylene, aryl or heterocyclyl radicals.

14. A chain extender as claimed in claim 13 wherein said alkenylene radicals are the alkenylene equivalent of the alkenyl radicals claimed in claim 3 or claim 4.

15. A chain extender as claimed in claim 13 wherein said alkenylene radicals are the alkenylene equivalent of the alkenyl radicals claimed in claim 5 or claim 6.

16. A chain extender as claimed in claim 13 wherein said alkynylene radicals are the alkynylene equivalent of the alkynyl radicals claimed in

claim 7 or claim 8.

17. A chain extender as claimed in claim 13 wherein said aryl radicals include single, polynuclear, conjugated and fused residues of aromatic hydrocarbons.

18. A chain extender as claimed in claim 17 wherein said aryl residues include phenyl, biphenyl, terphenyl, quaterphenyl, phenoxyphenyl, naphthyl, tetrahydronaphthyl, anthracenyl, dihydroanthracenyl, benzanthracenyl, dibenzanthracenyl, and phenanthrenyl.

19. A chain extender as claimed in claim 13 wherein said heterocycle radicals include mono- or poly-cyclic heterocyclyl groups containing at least one heteroatom selected from nitrogen, sulphour and oxygen.

20. A chain extender as claimed in claim 19 wherein said heterocycle radicals include N-containing heterocyclic groups, such as, unsaturated 3 to 6 membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl or tetrazolyl; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms, such as pyrrolidinyl, imidazolidinyl, piperidino or piperazinyl; unsaturated condensed heterocyclic groups containing 1 to 5 nitrogen atoms, such as, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl or tetrazolopyridazinyl; unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, such as, pyranyl or furyl; unsaturated 3 to 6-membered hetermonocyclic group containing 1 to 2 sulphur atoms, such as, thienyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, oxazolyl, isoazolyl or oxadiazolyl; saturated 3 to 6-membered

heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, morpholinyl; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, such as, benzoxazolyl or benzoxadiazolyl; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as thiazolyl or thiadiazolyl; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as, thiadiazolyl; and unsaturated condensed heterocyclic group containing 1 to 2 sulphur atoms and 1 to 3 nitrogen atoms, such as benzothiazolyl or benzothiadiazolyl.

21. A chain extender as claimed in any one of claims 1 to 20 wherein R_7 is a divalent linking group selected from O, S, and NR wherein R is hydrogen or an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical.

22. A chain extender as claimed in any one of the preceding claims wherein said optionally substituted radicals are substituted with one or more groups selected from oxygen, nitrogen, sulphur, alkyl, alkenyl, alkynyl, aryl, halo, haloalkyl, haloalkenyl, haloalkynyl, haloaryl, hydroxy, alkoxy, alkenyloxy, alkynyloxy, aryloxy, carboxy, benzyloxy, haloalkoxy, haloalkenyloxy, haloalkynyloxy, haloaryloxy, nitro, nitroalkyl, nitroalkenyl, nitroalkynyl, nitroaryl, nitroheterocyclyl, azido, amino, alkylamino, alkenylamino, alkynylamino, arylamino, benzylamino, acyl, alkenylacyl, alkynylacyl, arylacyl, acylamino, acyloxy, aldehydo, alkylsulphonyl, arylsulphonyl, alkylsulphonylamino, arylsulphonylamino, alkylsulphonyloxy, arylsulphonyloxy, heterocyclyl, heterocycloxy, heterocyclylamino, haloheterocyclyl, alkylsulphenyl, arylsulphenyl, carboalkoxy, carboaryloxy, mercapto, alkylthio, arylthio and acylthio.

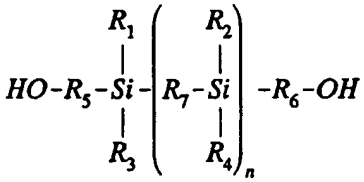
23. A chain extender as claimed in any one of the preceding claims wherein said silicon-containing diol is 1,3-bis(4-hydroxybutyl)tetramethyl disiloxane or 1,4-bis(3-hydroxypropyl)tetramethyl disilylethylene and 1-4-bis(3-hydroxypropyl)tetramethyl disiloxane.

24. A chain extender as claimed in any one of the preceding claims further including at least one other chain extender.

25. A chain extender as claimed in claim 24 wherein the at least one other chain extender is selected from 1,4-butanediol, 1,6-hexanediol, 1,8-octanediol, 1,9-nonanediol, 1,10-decanediol, 1,12-dodecanediol, 1,4-cyclohexanedimethanol, p-xylene glycol and 1,4-bis(2-hydroxyethoxy) benzene.

26. A chain extender as claimed in claim 25 or claim 26 wherein the silicon-containing diol is present in the chain extender in an amount of from 1 to 50 molar percent.

27. A silicon-containing diol of formula (I)



(I)

wherein

R_1, R_2, R_3, R_4, R_5, and R_6 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical;

R_7 is ethylene; and

n is 0 or greater, preferably 2 or less.

28. A polyurethane elastomeric composition including a chain extender or chain extender composition as claimed in any one of claims 1 to 26.

29. A polyurethane composition comprising a reaction product of:

(i) a soft segment macrodiol;

(ii) a diisocyanate; and

(iii) a chain extender as claimed in any one of claims 1 to 26.

30. A polyurethane composition as claimed in claim 29 wherein said soft segment macrodiol is selected from polyethers, polyesters, polysiloxanes, polycarbonates or mixtures thereof.

31. A polyurethane composition as claimed in claim 30 wherein the soft segment macrodiol is derived from a polysiloxane macrodiol and a polyether macrodiol.

32. A polyurethane composition as claimed in claim 30 wherein the soft segment macrodiol comprises a polysiloxane macrodiol having a molecular weight in the range of 200 to 5000.

33. A polyurethane composition as claimed in claim 31 wherein the molecular weight of the macrodiol is in the range of 300 to 1200.

34. A polyurethane composition as claimed in claim 30, 32 or 33 wherein the soft segment macrodiol is derived from polydimethyl siloxane.

35. A polyurethane composition as claimed in claim 30 wherein the soft segment macrodiol includes a polyether macrodiol of formula (II):

$$HO-[(CH_2)_m-O]_n-H$$

(II)

wherein
m is an integer of 5 or more; and
n is an integer of 2 to 50.

36. A polyurethane composition as claimed in claim 35 wherein m is from 5 to 18.

37. A polyurethane composition as claimed in claim 35 or claim 36 wherein the molecular weight of the polyether macrodiol is from about 200 to about 5000.

38. A polyurethane composition as claimed in claim 37 wherein the molecular weight of the polyether macrodiol is from about 200 to about 1200.

39. A polyurethane composition as claimed in any one of claims 29 to 30 wherein the diisocyanate is selected from 4,4'-methylenediphenyl diisocyanate (MDI), methylene bis(cyclohexyl) diisocyanate (H12MDI), p-phenylene diisocyanate (p-PDI), trans-cyclohexane-1, 4-diisocyanate (CHDI) or a mixture of the cis and trans isomers, 1,6-hexamethylene diisocyanate (DICH), 2,4-toluene diisocyanate (2,4-TDI) or its isomers or mixtures thereof, p-tetramethylxylene diisocyanate (p-TMXDI) and m-tetramethylxylene diisocyanate (m-TMXDI).

40. A polyurethane elastomeric composition comprising a reaction product of:

(i) macrodiols including:

(a) polysiloxane macrodiol; and

(b) polyether macrodiol;

(ii) MDI; and

(iii) chain extender composition including 1,4-butanediol and a silicon chain extender selected from 1,3-bis(4-hydroxybutyl)tetramethyl disiloxane and 1,4-bis(3-hydroxypropyl)tetramethyl disilylethylene and 1-4-bis(3-hydroxypropyl)tetramethyl disiloxane.

41. A polyurethane composition as claimed in claim 40 wherein the silicon chain extender is present in an amount of about 40 mol% of the chain extender composition.

42. A polyurethane composition as claimed in any one of claims 29 to 41 wherein the weight percentage of (diisocyanate plus chain extender) in the composition is from 20 to 60 wt%.

43. A polyurethane composition as claimed in claim 40 wherein the weight ratio of polysiloxane to polyether is from 1:99 to 99:1.

44. A polyurethane composition as claimed in claim 43 wherein the weight ratio of polysiloxane to polyether is about 80:20.

45. A biomaterial comprising a polyurethane elastomeric composition as claimed in any one of claims 29 to 44.

46. A medical device, article or implant composed wholly of partly of the polyurethane elastomeric composition as claimed in any one of claims 29 to 44.

47. A medical device, article or implant as claimed in claim 46 wherein the medical device, article or implant is selected from cardiac pacemakers, defibrillators and other electromedical devices, catheters, cannulas, implantable prostheses, cardiac assist devices, heart valves, vascular grafts, stents, extra-corporeal devices, artificial organs, pacemaker leads, defibrillator leads, blood pumps, balloon pumps, A-V shunts, biosensors, membranes for cell encapsulation, drug delivery devices, wound dressings, artificial joints, orthopaedic implants and soft tissue replacements.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00546

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: C07F 7/08 C08G 18/38

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC C07F 7/08 C08G 18/32, 18/38

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT: IPC + keywords

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 98/13405 A (CARDIAC CRC NOMINEES PTY LTD et al) 2 April 1998 See whole document	1-47
X	US 4647643 A (Zdrahala et al) 3 March 1987 See abstract, claims	1-12, 21, 28
X	JP 4-025580 A (TOYODA GOSEI KK) 29 January 1992 & Derwent Abstract Accession Number 92-083741	1-12, 21, 28

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 September 1998	18 SEP 1998
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929	Authorized officer **MATTHEW FRANCIS** Telephone No.: (02) 6283 2424

Form PCT/ISA/210 (second sheet) (July 1998) copjhw

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00546

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Derwent Abstract Accession No. 91-026349, Class A26, G02, JP 02-296832 A (HITACHI MAXELL) 7 February 1990	1-12, 21, 28
X	Derwent Abstract Accession No. 86-194758, Class A96, D21, E11, JP 61-129187 A (NISSHIN OIL MILLS KK) 17 June 1986	1-12, 21
X	Derwent Abstract accession No. 92-099871, Class A41, E11, JP 04-041493 A (SHINETSU CHEM IND KK) 19 February 1992	1-12, 21
X	GB 2092607 A (RCA Corporation) 18 August 1992 See whole document	1-12, 21
X	EP 385732 A (SHIN-ETSU Chemical Co., Ltd.) 5 September 1990 See abstract	1-12, 21
X	EP 464844 A (MERRELL DOW PHARMACEUTICALS INC) 8 January 1992 See claims	1-12, 21

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/AU 98/00546

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	9813405	AU	41924/97				
GB	2092607	DE	3202493	FR	2499284	JP	57150694
		US	4355062	US	4391720		
EP	385732	JP	2225524	US	5130460		
EP	464844	CN	1057842	AU	80114/91	CA	2046050
		FI	913253	HU	58748	IL	98711
		JP	4230394	NO	912629	NZ	238807
		PT	98219	ZA	9105075	US	5281738
		US	5304668				

END OF ANNEX